

## REMARKS

Claims 15 and 16 are pending in this application. No new matter is added.

Applicants note with appreciation the Examiner's withdrawal of the 35 U.S.C. § 112 rejections.

## CLAIM REJECTIONS

### Rejections under 35 U.S.C. §103

#### Combinations

Claims 15 and 16 are rejected under 35 U.S.C. §103(a), as being unpatentable over U.S. Patent 5,853,703 to Cerami ("Cerami") in view of U.S. Patent Publication 2002/0004500 to Reeves ("Reeves").

In the Office Action mailed January 12, 2006 ("Office Action"), the Examiner states that "Cerami et al. disclose a method of inhibiting and reversing protein aging by administering to a patient in need thereof an effective amount of a thiazolium compound represented by Formula (1)", and that "Cerami et al. teach that the method has therapeutic applications and that the thiazolium compound can be used in a method for treating hypertension. A preferred compound used in the therapeutic method is 3-(2-phenyl-2-oxoethyl)-4,5-dimethyl-thiazolium bromide." See Office Action at page 3. The Examiner further states that "Cerami et al. do not disclose combining the preferred compound with hydrochlorothiazide."

The Examiner "refers to Reeves et al., which teach that hydrochlorothiazide is one of several suitable agents that can be used to treat systolic hypertension." Office Action at page 3.

The Examiner states on page 4 of the office action that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify Cerami et al. by combining the thiazolium compound with hydrochlorothiazide because one of ordinary skill in the art would reasonably expect the additive effect of the two compounds to be effective in treating hypertension, especially isolated systolic hypertension."

Applicants respectfully disagree.

Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness with regard to the Cerami and Reeves references. A *prima facie* case of obviousness requires some suggestion or motivation, either in the references themselves or in the knowledge generally available in the art, to modify the reference or to combine reference teachings. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See also MPEP 706.02(j).

The instant claims relate to a method of treating, ameliorating or preventing isolated systolic hypertension in an animal, including a human by administering an effective amount of 3-(2-phenyl-2-oxoethyl)-4,5-dimethylthiazolium salt and an effective amount of hydrochlorothiazide.

Cerami relates to thiazolium compositions and methods for inhibiting and reversing nonenzymatic cross-linking (protein aging). See, e.g., Abstract.

Reeves describes vasopeptidase inhibitors useful in treating systolic hypertension. See, e.g., Abstract. Such compositions can be used in combination with "diuretics such as hydrochlorothiazide." See paragraph [0015].

There is no mention of hydrochlorothiazide in Cerami. Thus, there is no teaching or suggestion in Cerami that would motivate the skilled artisan to produce a combination of the compounds of the invention with hydrochlorothiazide for treating, ameliorating or preventing isolated systolic hypertension. Reading Cerami, one of ordinary skill in the art would not be motivated to look to the vasopeptidase inhibitor combination art (e.g., Reeves) for teaching of which types of compounds to combine with the thiazolium compositions of Cerami.

Further, mere disclosure of a combination of a vasopeptidase inhibitor and hydrochlorothiazide, without more, would not lead one of ordinary skill in the art to combine a 3-(2-phenyl-2-oxoethyl)-4,5-dimethylthiazolium salt and hydrochlorothiazide.

The fact that references can be modified or combined does not render the resulting combination obvious unless the prior art also suggests the desirability of the combination.

(See MPEP §2143.01, citing *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990)). In moving from the prior art to the claimed invention, one cannot base a determination of obviousness on what the skilled artisan might try or find obvious to *try*. Rather, the proper test requires determining what the prior art would have led the skilled artisan to *do*. As described above, there is no suggestion in Cerami that would motivate a skilled artisan to modify the compositions described therein.

Moreover, an assertion that modifying the Cerami reference would have been within the ordinary skill of the art at the time the claimed invention was made because the cited references were individually known in the art at the time the instant application was filed is also insufficient to establish a *prima facie* case of obviousness without some objective reason to combine the references. (See MPEP §2143.01, citing *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pate. App. & Inter. 1993)). Thus, the mere fact that the Cerami and Reeves references were known in the art individually at the time the instant application was filed does not render the claimed invention obvious, as there is no teaching or suggestion in the Cerami reference that would motivate one of ordinary skill in the art to modify the compounds and methods described therein by forming combinations with agents disclosed in Reeves as suitable for forming combinations with a vasopectidase inhibitor. Therefore, Applicants respectfully request withdrawal of this rejection.

#### Counterion

The Examiner states that it “would have been obvious to one of ordinary skill in the art at the time the invention was made to administer 3-(2-phenyl-2-oxoethyl)-4,5-dimethyl-thiazolium chloride because, in view of Cerami et al.’s teaching, one of ordinary skill in the art would reasonably expect the chloride compound to be effective in treating hypertension.” Office Action at page 4.

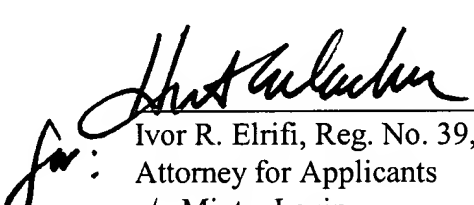
Cerami relates to thiazolium compositions and methods for inhibiting and reversing nonenzymatic cross-linking (protein ageing). However, the instant claims relate to a method of treating, ameliorating or preventing isolated systolic hypertension in an animal

by administering *a combination of* 3-(2-phenyl-2-oxoethyl)-4,5-dimethylthiazolium chloride or bromide *and* hydrochlorothiazide. There is no mention of hydrochlorothiazide in Cerami. There is no teaching or suggestion in Cerami of using a combination of the compounds of the invention (regardless of the nature of the counterion) with hydrochlorothiazide for treating, ameliorating or preventing isolated systolic hypertension. Therefore, Applicants respectfully request withdrawal of this rejection.

### CONCLUSION

On the basis of the foregoing amendment and remarks, Applicants respectfully submit that the pending claims are in condition for allowance and a Notice of Allowance for the pending claims is respectfully requested. If there are any questions regarding this application that can be handled in a phone conference with Applicants' Attorneys, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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